

WHAT IS CLAIMED IS:

1 1. A method of treating rheumatoid arthritis which comprises delivery of
2 a DNA sequence within a mammalian host, said DNA sequence expressing a biologically
3 active gene product such that said biologically active gene product imparts systemic relief
4 from rheumatoid arthritis.

1 2. The method of claim 1 wherein said DNA sequence is delivered
2 systemically within said mammalian host.

1 3. The method of claim 1 wherein said DNA sequence is delivered
2 locally within mammalian host.

1 4. The method of claim 2 wherein said DNA sequence encodes an
2 interleukin-1 receptor antagonist protein or a biologically active fragment thereof.

1 5. The method of claim 4 wherein said DNA sequence is transfected into
2 a hematopoietic cell-containing population.

1 6. The method of claim 5 wherein said hematopoietic cell-containing
2 population comprises bone marrow cells.

1 7. The method of claim 5 wherein said hematopoietic cell-containing
2 population comprises CD34⁺ blood leukocytes.

1 8. The method of claim 4 wherein the DNA sequence is transduced into
2 peripheral blood cells.

1 9. The method of claim 8 wherein said peripheral blood cells are
2 lymphocytes.

1 10. The method of claim 4 wherein said DNA sequence is subcloned into a
2 viral vector selected from the group consisting of a retroviral vector, an adenovirus vector, an
3 adeno-associated vector, a herpes simplex virus vector, an SV40 vector, a polyoma virus
4 vector, a papilloma virus vector, a picornavirus vector, and a vaccinia virus vector.

1 11. The method of claim 10 wherein said DNA sequence is transduced into
2 a hematopoietic cell-containing population.

1 12. The method of claim 11 wherein said hematopoietic cell-containing
2 population comprises bone marrow cells.

1 13. The method of claim 11 wherein said hematopoietic cell-containing
2 population comprises CD34⁺ blood leukocytes.

1 14. The method of claim 10 wherein the DNA sequence is transduced into
2 peripheral blood cells.

1 15. The method of claim 14 wherein said peripheral blood cells are
2 lymphocytes.

1 16. The method of claim 10 wherein said viral vector is a retroviral vector.

1 17. The method of claim 16 wherein said retroviral vector is transduced
2 into a hematopoietic cell-containing population.

1 18. The method of claim 17 wherein said hematopoietic cell-containing
2 population comprises bone marrow cells.

1 19. The method of claim 17 wherein the hematopoietic cell-containing
2 population comprises CD34⁺ blood leukocytes.

1 20. The method of claim 16 wherein the DNA sequence is transduced into
2 peripheral blood cells.

1 21. The method of claim 20 wherein said peripheral blood cells are
2 lymphocytes.

1 22. The method of claim 16 wherein said retroviral vector is MFG-IRAP.

1 23. The method of claim 22 wherein MFG-IRAP is used to transduce a
2 hematopoietic cell-containing population.

1 24. The method of claim 23 wherein said hematopoietic cell-containing
2 population comprises bone marrow cells.

1 25. The method of claim 23 wherein said hematopoietic cell-containing
2 population comprises CD34⁺ blood leukocytes.

1 26. The method of claim 22 wherein the DNA sequence is transduced into
2 peripheral blood cells.

1 27. The method of claim 26 wherein said peripheral blood cells are
2 lymphocytes.

1 28. The method of claim 3 wherein said DNA sequence encodes an
2 interleukin-1 receptor antagonist protein or a biologically active fragment thereof.

1 29. The method of claim 28 wherein said DNA sequence is transfected
2 into *in vitro* cultured myoblast cells and transplanted into said mammalian host.

1 30. The method of claim 29 wherein said DNA sequence is subcloned into
2 a non-viral vector.

1 31. The method of claim 30 wherein said non-viral vector is a plasmid
2 DNA vector.

1 32. The method of claim 29 wherein said DNA sequence is subcloned into
2 a viral vector.

1 33. The method of claim 32 wherein said DNA sequence is subcloned into
2 a retroviral vector.

1 34. The method of claim 33 wherein said retroviral vector is MFG-IRAP.

1 35. The method of claim 28 wherein said DNA sequence is injected
2 directly into skeletal muscle of said mammalian host.

1 36. The method of claim 35 wherein said DNA sequence is subcloned into
2 a non-viral vector.

1 37. The method of claim 36 wherein said non-viral vector is a plasmid
2 DNA vector.

1 38. The method of claim 35 wherein said DNA sequence is subcloned into
2 a viral vector.

1 39. The method of claim 38 wherein said DNA sequence is subcloned into
2 a retroviral vector.

1 40. The method of claim 39 wherein said retroviral vector is MFG-IRAP.

1 41. The method of claim 2 wherein said DNA sequence encodes a
2 cytokine or biologically active fragment thereof selected from the group consisting of
3 interleukin-4 and interleukin-10.

1 42. The method of claim 2 wherein said DNA sequence encodes a soluble
2 cytokine receptor or biologically active fragment thereof selected from the group consisting
3 of a soluble interleukin-1 receptor and a tumor necrosis factor- α soluble receptor.

1 43. The method of claim 2 wherein said DNA sequence encodes TIMP or
2 a biologically active fragment thereof.

1 44. The method of claim 2 wherein said DNA sequence encodes an anti-
2 adhesion molecule or a biologically active fragment thereof selected from the group
3 consisting of soluble ICAM-1, soluble CD44, and soluble CD18.

1 45. The method of claim 2 wherein said DNA sequence encodes
2 superoxide dismutase or a biologically active fragment thereof.

1 46. The method of claim 2 wherein said DNA sequence encodes a
2 cartilage growth factor or a biologically active fragment thereof selected from the group
3 consisting of IGF- α and TGF- β .

1 47. The method of claim 2 wherein said DNA sequence encodes collagen
2 or a biologically active fragment thereof.

1 48. The method of claim 3 wherein said DNA sequence encodes a
2 cytokine or biologically active fragment thereof selected from the group consisting of
3 interleukin-4 and interleukin-10.

1 49. The method of claim 3 wherein said DNA sequence encodes a soluble
2 cytokine receptor or biologically active fragment thereof selected from the group consisting
3 of the soluble interleukin-1 receptor and the tumor necrosis factor- α soluble receptor.

1 50. The method of claim 3 wherein said DNA sequence encodes TIMP or
2 a biologically active fragment thereof.

1 51. The method of claim 3 wherein said DNA sequence encodes an anti-
2 adhesion molecule or a biologically active fragment thereof selected from the group
3 consisting of soluble ICAM-1, soluble CD44, and soluble CD18.

1 52. The method of claim 3 wherein said DNA sequence encodes
2 superoxide dismutase or a biologically active fragment thereof.

1 53. The method of claim 3 wherein said DNA sequence encodes a
2 cartilage growth factor or a biologically active fragment thereof selected from the group
3 consisting of IGF- α and TGF- β .

1 54. The method of claim 3 wherein said DNA sequence encodes collagen
2 or a biologically active fragment thereof.

1 55. A method of treating systemic lupus erythematosus which comprises
2 delivery of a DNA sequence within a mammalian host, said DNA sequence expressing a
3 biologically active gene product such that said biologically active gene product imparts
4 systemic relief from systemic lupus erythematosus.

1 56. The method of claim 55 wherein said DNA sequence is delivered
2 systemically within said mammalian host.

1 57. The method of claim 55 wherein said DNA sequence is delivered
2 locally within said mammalian host.

1 58. The method of claim 56 wherein said DNA sequence encodes an
2 interleukin-1 receptor antagonist protein or a biologically active fragment thereof.

1 59. The method of claim 58 wherein said DNA sequence is transduced into
2 a hematopoietic cell-containing population.

1 60. The method of claim 59 wherein said hematopoietic cell-containing
2 population are bone marrow cells.

1 61. The method of claim 59 wherein said hematopoietic cell-containing
2 population comprise CD34⁺ blood leukocytes.

1 62. The method of claim 58 wherein the DNA sequence is transduced into
2 peripheral blood cells.

1 63. The method of claim 62 wherein said peripheral blood cells are
2 lymphocytes.

1 64. The method of claim 58 wherein said DNA sequence is subcloned into
2 a viral vector selected from the group consisting of a retroviral vector, an adenovirus vector,
3 an adeno-associated vector, a herpes simplex virus vector, an SV40 vector, a polyoma virus
4 vector, a papilloma virus vector, a picornavirus vector, and a vaccinia virus vector.

1 65. The method of claim 64 wherein said DNA sequence is transduced into
2 a hematopoietic cell-containing population.

1 66. The method of claim 65 wherein said hematopoietic cell-containing
2 population comprises bone marrow cells.

1 67. The method of claim 65 wherein said hematopoietic cell-containing
2 population comprises CD34⁺ blood leukocytes.

1 68. The method of claim 64 wherein the DNA sequence is transduced into
2 peripheral blood cells.

1 69. The method of claim 68 wherein said peripheral blood cells are
2 lymphocytes.

1 70. The method of claim 64 wherein said viral vector is a retroviral vector.

1 71. The method of claim 70 wherein said retroviral vector is transfected
2 into a hematopoietic cell-containing population.

1 72. The method of claim 71 wherein said hematopoietic cell-containing
2 population comprises bone marrow cells.

1 73. The method of claim 71 wherein the hematopoietic cell-containing
2 population comprises CD34⁺ blood leukocytes.

1 74. The method of claim 70 wherein the DNA sequence is transduced into
2 peripheral blood cells.

1 75. The method of claim 74 wherein said peripheral blood cells are
2 lymphocytes.

1 76. The method of claim 70 wherein said retroviral vector is MFG-IRAP.

1 77. The method of claim 76 wherein MFG-IRAP is used to transduce a
2 hematopoietic cell-containing population.

1 78. The method of claim 77 wherein said hematopoietic cell-containing
2 population comprises bone marrow cells.

1 79. The method of claim 77 wherein said hematopoietic cell-containing
2 population comprises CD34⁺ blood leukocytes.

1 80. The method of claim 76 wherein the DNA sequence is transfected into
2 peripheral blood cells.

1 81. The method of claim 80 wherein said peripheral blood cells are
2 lymphocytes.

1 82. The method of claim 57 wherein said DNA sequence encodes an
2 interleukin-1 receptor antagonist protein or a biologically active fragment thereof.

1 83. The method of claim 82 wherein said DNA sequence is transfected
2 into *in vitro* cultured myoblast cells and transplanted into said mammalian host.

1 84. The method of claim 83 wherein said DNA sequence is subcloned into
2 a non-viral vector.

1 85. The method of claim 84 wherein said non-viral vector is a plasmid
2 DNA vector.

1 86. The method of claim 83 wherein said DNA sequence is subcloned into
2 a viral vector selected from the group consisting of a retroviral vector, an adenovirus vector,
3 an adeno-associated vector, a herpes simplex virus vector, an SV40 vector, a polyoma virus
4 vector, a papilloma virus vector, a picornavirus vector, and a vaccinia virus vector.

1 87. The method of claim 86 wherein said DNA sequence is subcloned into
2 a retroviral vector.

1 88. The method of claim 87 wherein said retroviral vector is MFG-IRAP.

1 89. The method of claim 82 wherein said DNA sequence is injected
2 directly into skeletal muscle of said mammalian host.

1 90. The method of claim 89 wherein said DNA sequence is subcloned into
2 a non-viral vector.

1 91. The method of claim 90 wherein said non-viral vector is a plasmid
2 DNA vector.

1 92. The method of claim 89 wherein said DNA sequence is subcloned into
2 a viral vector selected from the group consisting of a retroviral vector, an adenovirus vector,
3 an adeno-associated vector, a herpes simplex virus vector, an SV40 vector, a polyoma virus
4 vector, a papilloma virus vector, a picornavirus vector, and a vaccinia virus vector.

1 93. The method of claim 92 wherein said DNA sequence is subcloned into
2 a retroviral vector.

1 94. The method of claim 93 wherein said retroviral vector is MFG-IRAP.

1 95. The method of claim 56 wherein said DNA sequence encodes a
2 cytokine or biologically active fragment thereof selected from the group consisting of
3 interleukin-4 and interleukin-10.

1 96. The method of claim 56 wherein said DNA sequence encodes a soluble
2 cytokine receptor or biologically active fragment thereof selected from the group consisting
3 of the soluble interleukin-1 receptor and the tumor necrosis factor- α soluble receptor.

1 97. The method of claim 56 wherein said DNA sequence encodes TIMP or
2 a biologically active fragment thereof.

1 98. The method of claim 56 wherein said DNA sequence encodes an anti-
2 adhesion molecule or a biologically active fragment thereof selected from the group
3 consisting of soluble ICAM-1, soluble CD44, and soluble CD18.

1 99. The method of claim 56 wherein said DNA sequence encodes
2 superoxide dismutase or a biologically active fragment thereof.

1 100. The method of claim 56 wherein said DNA sequence encodes a
2 cartilage growth factor or a biologically active fragment thereof selected from the group
3 consisting of IGF- α and TGF- β .

1 101. The method of claim 56 wherein said DNA sequence encodes collagen
2 or a biologically active fragment thereof.

1 102. The method of claim 57 wherein said DNA sequence encodes a
2 cytokine or biologically active fragment thereof selected from the group consisting of
3 interleukin-4 and interleukin-10.

1 103. The method of claim 57 wherein said DNA sequence encodes a soluble
2 cytokine receptor or biologically active fragment thereof selected from the group consisting
3 of a soluble interleukin-1 receptor and a tumor necrosis factor- α soluble receptor.

1 104. The method of claim 57 wherein said DNA sequence encodes TIMP or
2 a biologically active fragment thereof.

1 105. The method of claim 57 wherein said DNA sequence encodes an anti-
2 adhesion molecule or a biologically active fragment thereof selected from the group
3 consisting of soluble ICAM-1, soluble CD44, and soluble CD18.

1 106. The method of claim 57 wherein said DNA sequence encodes
2 superoxide dismutase or a biologically active fragment thereof.

1 107. The method of claim 57 wherein said DNA sequence encodes a
2 cartilage growth factor or a biologically active fragment thereof selected from the group
3 consisting of IGF- α and TGF- β .

1 108. The method of claim 57 wherein said DNA sequence encodes collagen
2 or a biologically active fragment thereof.

1 109. A method of treating osteogenesis imperfecta which comprises
2 delivery of a DNA sequence encoding collagen or a biologically active fragment thereof
3 within a mammalian host so as to promote therapeutic relief from osteogenesis imperfecta.

1 110. The method of claim 109 wherein said DNA sequence is delivered
2 systemically within said mammalian host.

1 111. The method of claim 110 wherein said DNA sequence is subcloned
2 into a viral vector selected from the group consisting of a retroviral vector, an adenovirus
3 vector, an adeno-associated vector, a herpes simplex virus vector, an SV40 vector, a polyoma
4 virus vector, a papilloma virus vector, a picornavirus vector, and a vaccinia virus vector.

1 112. The method of claim 111 wherein said viral vector is a retroviral
2 vector.

1 113. A method of treating osteoporosis which comprises delivery of a DNA
2 sequence within a mammalian host, said DNA sequence expressing a biologically active gene
3 product such that said biologically active gene product imparts systemic relief from
4 osteoporosis.

1 114. The method of claim 113 wherein said DNA sequence is delivered
2 systemically within said mammalian host.

1 115. The method of claim 114 wherein said DNA sequence is subcloned
2 into a viral vector selected from the group consisting of a retroviral vector, an adenovirus
3 vector, an adeno-associated vector, a herpes simplex virus vector, an SV40 vector, a polyoma
4 virus vector, a papilloma virus vector, a picornavirus vector, and a vaccinia virus vector.

1 116. The method of claim 115 wherein said viral vector is a retroviral
2 vector.

1 117. The method of claim 116 wherein said DNA sequence encodes a
2 cytokine or biologically active fragment thereof selected from the group consisting of
3 interleukin-1 receptor antagonist, interleukin-4 and interleukin-10.

1 118. The method of claim 116 wherein said DNA sequence encodes a
2 soluble cytokine receptor or biologically active fragment thereof selected from the group
3 consisting of a soluble interleukin-1 receptor, a tumor necrosis factor- α soluble receptor and a
4 soluble interleukin-6 receptor.

1 119. The method of claim 116 wherein said DNA sequence encodes TIMP
2 or a biologically active fragment thereof.

1 120. The method of claim 116 wherein said DNA sequence encodes an anti-
2 adhesion molecule or a biologically active fragment thereof selected from the group
3 consisting of soluble ICAM-1, soluble CD44, and soluble CD18.

1 121. The method of claim 116 wherein said DNA sequence encodes
2 superoxide dismutase or a biologically active fragment thereof.

1 122. A method of treating a connective tissue disease or disorder selected
2 from the group consisting of Sjögren's syndrome, polymyositis-dermatomyositis, systemic
3 sclerosis, vasculitis syndromes, juvenile rheumatoid arthritis, ankylosing spondylitis,
4 psoriatic arthritis, osteoporosis, osteogenesis imperfecta, Paget's disease and inflammatory
5 bowel disease which comprises delivery of a DNA sequence within a mammalian host, said
6 DNA sequence expressing a biologically active gene product such that said biologically
7 active gene product imparts systemic relief from said connective tissue disease or disorder.

1 123. The method of claim 122 wherein said viral vector is a retroviral
2 vector.

1 124. The method of claim 123 wherein said DNA sequence encodes a
2 cytokine or biologically active fragment thereof selected from the group consisting of
3 interleukin-1 receptor antagonist, interleukin-4 and interleukin-10.

1 125. The method of claim 123 wherein said DNA sequence encodes a
2 soluble cytokine receptor or biologically active fragment thereof selected from the group
3 consisting of a soluble interleukin-1 receptor, a tumor necrosis factor- α soluble receptor and
4 a soluble interleukin-6 receptor.

1 126. The method of claim 123 wherein said DNA sequence encodes TIMP
2 or a biologically active fragment thereof.

1 127. The method of claim 123 wherein said DNA sequence encodes an anti-
2 adhesion molecule or a biologically active fragment thereof selected from the group
3 consisting of soluble ICAM-1, soluble CD44, and soluble CD18.

1 128. The method of claim 123 wherein said DNA sequence encodes
2 superoxide dismutase or a biologically active fragment thereof.

1 129. The method of claim 123 wherein said DNA sequence encodes a
2 cartilage growth factor or a biologically active fragment thereof selected from the group
3 consisting of IGF- α and TGF- β .

1 130. The method of claim 123 wherein said DNA sequence encodes
2 collagen or a biologically active fragment thereof.

1 131. A mammalian cell comprising a recombinant retroviral vector wherein
2 said recombinant retroviral vector comprises a DNA sequence encoding IRAP or a
3 biologically active fragment thereof.

1 132. A mammalian cell of claim 131 wherein said recombinant retroviral
2 vector is derived from a Moloney murine leukemia virus.

1 133. A mammalian cell of claim 132 where said DNA sequence encoding
2 IRAP or a biologically active fragment thereof consists essentially of SEQ ID NO:2.

1 134. A mammalian cell of claim 133 wherein said recombinant retroviral
2 vector is MFG-IRAP.

1 135. The mammalian cell of claim 131 which is a hematopoietic cell.

1 136. The mammalian cell of claim 132 which is a hematopoietic cell.

- 1 137. The mammalian cell of claim 133 which is a hematopoietic cell.
- 1 138. The mammalian cell of claim 134 which is a hematopoietic cell.
- 1 139. The hematopoietic cell of claim 135 which is a bone marrow cell.
- 1 140. The hematopoietic cell of claim 136 which is a bone marrow cell.
- 1 141. The hematopoietic cell of claim 137 which is a bone marrow cell.
- 1 142. The hematopoietic cell of claim 138 which is a bone marrow cell.